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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,044	09/02/2005	Robert Norman Barker	0380-P03549US0	6955

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EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
03/03/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,044	BARKER ET AL.	
	Examiner	Art Unit	
	AMY E. JUEDES	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-13 and 15-50* is/are pending in the application.

4a) Of the above claim(s) *3-5,8-13,15-40,44-46,48 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-7, 41-43, 47, and 49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks, filed 12/10/09, are acknowledged.

Claims 6-7 and 47 have been amended.

Claims 3-13 and 15-50 are pending.

Claims 3-5, 8-13, 15-40, 44-46, 48, and 50 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 6-7, 41-43, 47, and 49 are being acted upon.

2. The rejection of the claims under 35 U.S.C. 112 second paragraph is withdrawn in view of Applicant's amendment to the claims.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-7, 41-43, and 47 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of treatment/prophylaxis of autoimmune disease, atopic/allergic disease, or graft rejection comprising administering a target antigen and a tolerogenic peptide sequence from EBV encoded LMP1 or LMP2 protein, thereby inhibiting the immune response to the target antigen,

does not reasonably provide enablement for:

a method of prophylaxis/treatment of a disease or condition mediated by an immune response against a target antigen comprising administering a target antigen and a tolerogenic peptide sequence from EBV encoded LMP1 or LMP2 protein, thereby inhibiting the immune response to the target antigen.

As set forth previously, The specification disclosure is insufficient to enable one skilled in the art to

practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, *in re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

"The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling (MPEP 2164.03)" The MPEP further states that physiological activity can be considered inherently unpredictable.

The specification provides insufficient guidance to enable claims drawn to the method as broadly claimed. The instant claims are drawn to a method of prophylaxis or treatment of a disease or condition mediated by an immune response against a target antigen. This might encompass treating a broad range of diseases or conditions mediated by completely different pathological mechanisms. For example, the claims might encompass treating HIV, which is involves the destruction of HIV infected CD4 T cells (i.e. an "immune response against a target antigen"). However, as taught by Burgers et al., one of the primary goals of treating HIV involves inducing a sufficient immune response against the virus, and ability to treat HIV by inducing tolerance to target HIV antigens would thus be extremely unpredictable. Furthermore, the instant claims might encompass treating Alzheimer's disease, which involves (i.e. is mediated by) an immune response against target CNS antigens (see Mor et al., 2005). However, Mor et al. also teach that under certain circumstances the immune response against said target antigens might actually be protective and be involved in the clearance of amyloid deposits. Thus, inhibiting an immune response to Alzheimer's target antigens with the claimed method would be extremely unpredictable, since it might actually inhibit a protective immune response involved in clearing amyloid deposits.

Thus, given the breadth of the claims and the unpredictability of the art, the instant specification must provide a sufficient an enabling disclosure commensurate in scope with the instant claims. The instant specification demonstrates that various peptides of EBV1 encoded LMP1 and LMP2 can suppress the immune response to a target antigen in vitro, including to allergen or alloantigen target antigens. Given, the ability of the LMP1/LMP2 peptides to suppress the immune response to a target antigen, it would be reasonable to administer the LMP peptide and target antigens in vivo to suppress the immune response to the target antigen for treatment of autoimmune disease, allergy, or graft rejection. However, the instant specification does not provide any guidance regarding treating the diseases as broadly claimed (for example, Alzheimer's or HIV infection, which operate by completely different pathological mechanisms than autoimmune disease, allergy, or graft rejection). Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

Applicant's arguments filed 12/10/09 have been fully considered, but they are not persuasive.

Applicant argues that the amendment to the claims to recite that the method inhibits the immune response to a target antigen obviates the rejection.

However, the claims still encompass treating a broad range of diseases by inhibiting an immune response, which is extremely unpredictable. The specification does not provide sufficient guidance to treat the broad range of diseases encompassed by the instant claims, as noted above.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 6-7, 41-43, 47, and 49 stand rejected under 35 102(e) as being anticipated by U.S. Patent 6,642,008 (of record), as evidenced by Dukers et. al., 2000 (of record) and Wakiguchi et al., 2002.

As set forth previously, The '008 patent teaches administering EBV encoded LMP1 protein to a subject seropositive for EBV (see column 7-8 and 15, in particular). As evidenced by Dukers et al., said EBV encoded LMP1 protein comprises the sequence of peptide P4 of the instant application (see page 664 and Table I in particular, residues 16-35). The '008 patent also teaches that the LMP1 protein can be in the form of a fusion protein with other EBV proteins (i.e. a "target antigen", see column 15 in particular). Furthermore, the '008 patent teaches that immune response to EBV viral antigens correlates with diseases such as atopic disease (i.e. said diseases are mediated by an immune response against said viral "target antigens", see column 5 and 17 of the '008 patent, in particular). Additionally, as evidenced by Wakiguchi, 2002, mosquito allergy is associated with EBV (i.e. EBV is an antigen which provokes an allergic immune response). Thus, the EBV target antigens administered in the method of the '008 patent are inherently antigens which "provoke" an allergic immune response.

Applicant's arguments filed 12/10/09 have been fully considered, but they are not persuasive.

Applicant argues that the '008 patent teaches administering LMP1 protein for the purpose of eliciting the production of antibodies or to induce an immune response. Thus, Applicant concludes that the '008 patent does not teach inhibiting an immune response to the target antigen, as recited in the instant claims.

As an initial matter, it is noted that the recitation of inhibiting an immune response to the target antigen appears to pertain to the species of method wherein a nucleic acid encoding a tolerogenic peptide sequence is administered, such that the peptide is expressed in the individual. The species of method wherein a peptide is administered (i.e. the method of the '008 patent) does not appear to be limited to inhibiting an immune response. However, even if the instant claims were drawn to administering a tolerogenic peptide to inhibit an immune response to the target antigen, the '008 patent would still inherently anticipate the instant claims. The '008 patent teaches that the method can be performed for the immunotherapy of diseases associated with EBV, including atopic disease (see column 5, 17, and 20). While the '008 patent does teach that the LMP1 fusion proteins induce an antibody immune response, the instant claims are not limited to inhibiting an antibody response to a target antigen. Rather the claims encompass inhibiting any immune response to the target antigen (for example, a Th1 response, an APC response, and NK cell response, etc.). The instant specification demonstrates that LMP1 induces IL-10 in subjects previously infected with EBV, which in turn inhibits certain T cell immune responses. Thus, the ability to inhibit certain immune responses in subjects exposed to EBV is an inherent property of LMP1 protein. The '008 patent discloses administering an LMP1 protein, in combination with other "target antigens" to subjects exposed to EBV. Thus, the method of the '008 patent is identical to that of the instant claims, and would inherently result in the inhibition of some type of immune response, even if the method also results in the induction of an antibody response.

Applicant further argues that hypersensitivity to mosquito bites is not an allergic disease, as recited in the instant claims. Applicant cites Ishihara et al. as evidence of the fact that mosquito bite hypersensitivity is not an allergic disease.

As an initial matter, the limitation of an allergic disease is only relevant to claim

49, since claim 47 encompasses treatment of any disease mediated by an immune response against a target antigen by administering said target antigen. The Ishihara et al. reference cited by Applicant teaches that mosquito bite hypersensitivity is a lymphoproliferative disease associated with EBV (i.e. the reference teaches that EBV is a "target antigen" for an immune response that mediates a disease, as recited in claim 47). Regarding the limitations of claim 49, it is noted that the claim is drawn to administering a target antigen which provokes a disease comprising an atopic or allergic immune response. Irrespective of the teachings of Ishihara et al. regarding the role of EBV in mosquito bite hypersensitivity, it is noted that the '008 patent itself teaches that those harboring EBV virus are at risk of developing various diseases, including allergic disease, and that the disclosed method results in the treatment of said diseases (see column 4-5, in particular). Thus, based on the teachings of the '008 patent, EBV antigens can be considered "target antigens" which provoke an allergic immune response, as recited in claim 49.

5. No claim is allowed.

6. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-

4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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